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In Silico Design, Synthesis, and Toxicological Evaluation of 1,3-Thiazolidine-2,4-dione Derivatives as PPAR γ Agonists

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Thiazolidinediones (TZD) are ligands for PPAR γ used for the treatment of type. diabetes mellitus (DM2), though, drugs from this group have been shown to produce hepatic toxicity. The aim of this work is to design. new set of molecules based on the substitution of TZD with electro donating and electro withdrawing heteroatoms, which might activate the PPAR γ while minimizing the adverse effects. One hundred and thirty derivatives were design. The derivatives contained the polar head of TZD and an aromatic body which served simultaneously as the body and the tail. The physicochemical properties of the derivatives were evaluated using the Molinspiration software and Osiris Property Explorer. Additionally, docking studies were carried out using Autodock 4.0. Two ligands were selected in order to synthesize them through. Knoevenagel condensation, in. solvent free reaction. The products were identified using spectroscopic techniques. Acute oral toxicity was performed as per OECD 425 guideline (Up. Down method) using healthy female albino Wistar rats. It was found that the compounds are in accordance with Lipinski's rule of 5, and none of them are toxic according to the predictions. In the docking results, the interaction of the ligands was more likely when the derivatives were substituted with electro withdrawing heteroatoms since these enhanced the formation of hydrogen bonding between the head of compound and the ligand binding domain (LBD), leading to the selection of the best two compounds to be synthesized, which will be further mentioned as C40 and C81. C40 consists of the polar head and salicylaldehyde, while C81 consists of the polar head and chlorofluorobenzaldehyde. The proposed methodology was optimal for obtaining the desired products. The compounds were obtained with. yield of 98% and 67%, respectively. According to the toxicity study, it was found that C40 had. LD50 above 2000 mg/kg, while C81 had. LD50 between 700 and 1400 mg/kg.

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No-Touch technique with the use of total arterial revascularisation in elderly Diabetic patients decrease the postoperative morbidity

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Background: Our aim of this study was to compare the clinical outcomes after coronary artery by-pass grafting (CABG) operations in diabetic and non-diabetic elderly patients using with different surgical approaches.

Method: This study was performed between 2009 and 2015. 1300 patients (older than 70 yrs), who treated wit. insuline or oral antidiabetic drugs, were included. In all patients, we used arterial conduits. We compared postoperative outcomes of traditional CABG technique (G1; N=650), and On-Pump Beating Heart (OPBH) (G2). An aortic cross clamp and. side clamp as the main risk factors of peroperative cerebrovascular events was used in G1 patients. In G2, for institution of extracorporeal circulation, we used common femoral artery and. two-staged atrial cannulation for extracorporeal circulation (ECC).

Results: 39 patients (26 pts from G1(4%), 13 pts from G2 (2%)) died postoperatively (P=0.022). Postoperative complications have been detected in 166 patients (12.7%) in both groups. 102 patients were from Group1 (15.6%) (P=0.0001). We detected postoperative complications in 64 patients from G2 (9.8%) (P=0.001). Cerebrovascular events (CVE), LCOS, and postoperative renal impairment were more common complication in Group. (P=0001). CVE, renal failure, and LCOS requiring IABP were more common in G1 pts (18.4%) (P=0.001). Complications including stroke, peroperative myocardial infarction, and more than 48 hours mechanical ventilation because of respiratory distress syndrome were more common in G1 patients.

Conclusion: On-pump beating heart surgery without the use of aortic cross and side clamp decreased significantly postoperative complications in elderly patients who underwent total arterial CABG. Need for more than 48 hours mechanical ventilation, arrhythmia, mediastinitis, cerebrovascular events, and myocardial infarction after surgery were the most occurred complications in these particular group.

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